REMARKS

By the present amendment, claim 1 has been amended to delete the recitation that the coat "may be permeable or impermeable to water" and to recite that the core composition is "a compressed core composition," that the swelling agent is "selected from the group consisting of silicified microcrystalline cellulose, crospovidone, sodium starch glycolate, sodium croscarmellose, ion exchange resins and mixtures thereof," and that the swelling agent is present in the core composition "in an amount of from 5% to 95% by weight of the system."

Support for the added recitations is found in the application, for example, at least page 23, line 11, paragraph 0122 and the Examples (compressed), page 15, lines 23-26, paragraph 0098 (swelling agent), the Figures and Examples (film), and page 15, lines 26-27, paragraph 0098 (amount by weight).

Claim 3 has been amended to recite that the "the cover composition is a pH dependent polymer that is soluble in alkaline environment."

Support for the added recitation is found in the original application, for example, at least page 34, lines 6-7, paragraph 0155.

Claim 6 has been amended to recite that the composition used to cover the passageway "contains a water swellable polymer."

Support for the added recitation is found in the original application, for example, at least page 17, line 4, paragraph 0103.

Claims 16-18 and 22 have been canceled without admission, prejudice or disclaimer.

New claim 25 has been added to recite that the film is made from a coating solution after evaporation of a solvent.

Support for the added recitation is found in the original application, for example, at least the Examples.

Claims 1, 3-15, 19-21 and 23-25 are pending in the present application. Claim 1 is the only independent claim.

I. Obviousness rejection

In the Office Action, claims 1 and 3-24 are rejected under 35 U.S.C. 103(a) as obvious over US 6,004,582 to Faour et al. ("Faour") in view of US 5,229,131 to Amidon et al. ("Amidon").

Reconsideration and withdrawal of the rejection is respectfully requested.

Faour does not teach or suggest using a **swelling agent in the core of a type and in an amount so that there is a positive rupture of the coat**, upon contact with the aqueous environment, due to pressure exerted on the coat by the swelling agent.

In Faour, the device possesses a water-soluble coat that comprises a swelling agent, for example, crospovidone (see Faour at Examples 4 and 6). However, the core of Faour does not contain such a swelling agent.

Further, a person of ordinary skill in the art would not have had any incentive or motivation to modify Faour to add such a swelling agent in the core of Faour. First, there is no teaching or suggestion in Faour that the rupture of the semipermeable coating is desirable.

Second, the device of Faour is an osmotic device, and a person skilled in the art would have been aware that rupture of the coating is never a desirable functional feature for osmotic devices.

Reference is made to Annexures I and II submitted with this paper.

Annexure I is a standard textbook reference which confirms that osmotic drug delivery systems are meant for controlled, prolonged release over a period of time, and not a pulsed release wherein almost 100 % of the drug is released at one particular time point. Annexure II is another standard manual which states that for osmotic systems, "the delivery orifice must be properly sized to prevent internal pressures from exceeding the mechanical design limits of system components, could potentially result in system failure."

Thus, a person of ordinary skill in the art would not have been motivated to add in the core of Faour a swelling agent of a type and/or amount likely to cause a rupture of the coat, because this would have been considered a failure of the system of Faour.

In contrast, in the presently claimed invention, as recited in present claim 1, the core composition comprises at least one swelling agent **selected from the group consisting of silicified microcrystalline cellulose, crospovidone, sodium starch glycolate, sodium croscarmellose, ion exchange resins and mixtures thereof**.

Also, as recited in present claim 1, the swelling agent present in the core composition in **an amount of from 5% to 95% by weight of the system**, such that, when the system is exposed to an aqueous environment, the swelling agent swells and exerts a pressure on the coat, thereby rupturing the coat to release contents of the core composition.

The features of the presently claimed invention and their advantages are not taught or suggested in Faour, which does not use swelling agents of the type and amounts as in the presently claimed invention, and for which rupture of the coat would be considered a system failure. Further, Amidon concerns a different system that does not rely on a passageway in the coat (see Amidon "Summary of the Invention" starting at col. 4, lines 35), so the person of the art would not refer to Amidon in relation to the system of Faour**.** Therefore, the present claims are not obvious over Faour and Amidon taken alone or in any combination.

In addition, contrary to the assertion set forth in the Office Action, Faour does not teach or suggest a plug **substantially covering only the orifice or passageway**, in order to achieve a programmed drug delivery system. Namely, in Faour, the coat 3 "surrounds" at least a portion of the semi-permeable membrane 4 [see Faour col. 3, line 63 and col. 5, lines 6-8 and also col. 4, lines 56-59 which provides brief description of the figures. The term "surround" suggests the form of an "enclosure" around at least a portion of the membrane 4. Moreover, in all Examples of Faour the coating surrounds the membrane completely. Thus, it is submitted that the person of the art would understand "surrounding" as clearly indicating that the covering of the membrane 4 must be substantial.

It is noted that Faour, in its disclosure of the coat 3 (see col. 7, lines 12-15), incorporates by reference a textbook, i.e., Pharmaceutical Dosage Forms: Tablets, Volume I, Third Edition. A. Lieberman. Ed. 1989, Marcel Dekkar, Inc., which represents knowledge of a person of the art of pharmaceutical technology regarding coating processes. Copies of pages that generally

describe the general coating procedure from this textbook reference (Indian Ed.) are submitted as Annexure III.

The textbook does not give a slightest hint that the coating 3 may be applied to cover substantially only the passageway. On the contrary, the textbook's teaching is that the coat, not only covers the passageway, but also surrounds substantially the remaining surface of core substrate where there is no passageway.

Also, the coating equipment described in the textbook cited by Faour leads a person skilled in the art to understand that the coating composition is applied so that core is completely surrounded by the coating and there is no selective area on which it is coated. See, e.g., Annexure III at page 348, under Equipment. The different types of equipment that are available and used in the pharmaceutical art (such as the standard and perforated coating pan, fluidized coating apparatus and other automated equipment used in the coating process) are developed to achieve **smooth , uniform** coating around the tablet cores. See also Annexure III at page 360, 3rd paragraph ("[a] band of spray should be spread evenly over the tablet mass"). Further, on page 371, defects of film coating are identified, which mainly result from non-uniform distribution of the coating solution on the tablet surface.

Since Faour is silent regarding any adapted process or machine to cover substantially only the passageway, the person of the art would interpret this silence in both Faour and the textbook as a confirmation that the coat 3 of Faour inherently covers a substantial portion of the membrane 4.

Further, Amidon fails to remedy the deficiencies of Faour, because Amidon only teaches a conventional coating as follows (Amidon at col. 8, line 65 to col. 9, line 10):

> The unit cores are next coated with a solution of the desired coating polymer(s) in a solvent. The solvent may be organic, such as acetone, or in some embodiments, aqueous. Suitable machinery for coating include a rotating pan apparatus with a Sigma glass spray unit, a Uni-Glatt suspension coater or any other known fluidized bed equipment or pan coating technique typically used in the pharmaceutical industry. Next, the coated unit core is dried or cured for a predetermined time period at a predetermined temperature. The process variables, including spray rate, spray distance, atomization pressure, drying temperature and rate, and pan rotation speed, may effect the physical and mechanical properties of polymer coated drug cores.

Thus, both the textbook reference incorporated in Faour and Amidon fail completely to teach or suggest how to coat one specific area or portion of the substrate surface while leaving the other areas /surfaces of the substrate uncoated.

In contrast, in the presently claimed invention, as recited in present claim 1, the cover composition is **applied so as to substantially cover only the passageway**.

An advantage of this feature is that, in combination with the core containing the swelling agent, it facilitates a design of the system that makes it possible to obtain a complete rupture of the coating, so as to provide an effective pulse release of the whole dose of the active ingredient that is present in the compressed core. A system having such rupture property would not be possible with the "surrounding" coat 3 of Faour, in which rupture would be considered a failure of the osmotic system.

In summary, it is submitted that a person of ordinary skill in the art would not have been motivated to combine Faour with Amidon, and any combination of these references would not

have resulted in the presently claimed invention because of the lack of the specified swelling agent and/or because the plug of Faour is part of a coating that extends over a substantial portion of the membrane. Therefore, the present claims are not obvious over Faour and Amidon taken alone or in any combination.

In addition, with respect to the dependent claims, it is submitted that the combined features of each of these respective claims are not taught or suggested by the cited references. Therefore, each of the dependent claims is not obvious over Faour and Amidon taken alone or in any combination.

In view of the above, it is submitted that the rejection should be withdrawn.

II. Anticipation rejection

In the Office Action, claims 1-3-22 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by US 5,474,784 to Stevens et al. ("Stevens") as evidenced by US 5,229,131 to Amidon et al. ("Amidon").

Reconsideration and withdrawal of the rejection is respectfully requested.

First, contrary to the assertion at page 9 of the Office action, Stevens at col. 2, lines 18-20 does not suggest using PVP in the core. This passage of Stevens is at the end of a paragraph that describes materials for the plug, not the core (Stevens at col. 2, lines 7-20) (emphasis added):

> The water soluble or dispersable material is preferably one which can readily be formed into the configuration required for a particular device. Thus materials or blends of materials which are amenable to forming by direct powder compression or by wet granulation and compression or other such techniques are preferred for use in this invention. Those materials known to be useful as

> excipients in pharmaceutical tablets **are generally suitable for use in the formation of the plugs** useful in the devices of this invention. Examples of such materials include sugars such as lactose, sucrose, dextrose, sorbitol and mannitol; dextrins; polycarboxylic acids such as ascorbic acid, malic acid, fumaric acid, citric acid and tartaric acid; polyethylene glycols, **polyvinyl pyrrolidone**, and polyvinylacetate. **All of these materials can be compressed to form suitable plugs.**

This passage of Stevens is consistent with Examples 5 and 7 of Stevens, where PVP is used for the plug of the capsule (see Stevens at col. 7, line 6 and col. 8, line 25). In contrast, Stevens is completely silent regarding using PVP in the content of its capsule.

Moreover, in the presently claimed invention, as recited in present claim 1, not only the core contains a swelling agent, unlike the capsule content of Stevens, but in further contrast to Stevens, the swelling agent present in the core is **selected in the group consisting of silicified microcrystalline cellulose, crospovidone, sodium starch glycolate, sodium croscarmellose, ion exchange resins and mixtures thereof**, as recited in present claim 1.

An advantage of this feature in combination with the other features of the presently claimed invention is that, when the system is exposed to an aqueous environment, the swelling agent a pressure on the coat, thereby rupturing the coat to release contents of the core composition.

This feature of the presently claimed invention and the corresponding advantages are not taught or suggested in Stevens, especially since Stevens does not use swelling agents in the capsule apart from the plug. Therefore, the present claims are not anticipated by, and not obvious over, Stevens.

In addition, Stevens discloses a capsule which is a hollow device comprising a water impermeable wall or coat, with an orifice closed by the insertion of a plug which is soluble or dispersible in water. The plug of Stevens is in the form of a tablet with a suitable size and dimension to be able fit into the orifice or the open end of the hollow cylinder. Thus, Stevens teaches a **plug formed as a compressed tablet and not a cover composition applied as a film** onto the passageway of a compressed core (see Stevens at col. 2, lines 10-20 and all Examples).

More specifically, Stevens describes the construction of the device, which may be a hollow cylinder, as follows (Stevens at col 2, lines 61-67):

> A preferred form of a device according to this invention comprises a hollow cylinder open at one or both ends having a water impermeable construction, said device having a plug of water soluble or dispersable material inserted so as to close the open end or ends. Such devices may be readily formed, e.g. from an extruded plastic tube cut into lengths and optionally sealed at one end.

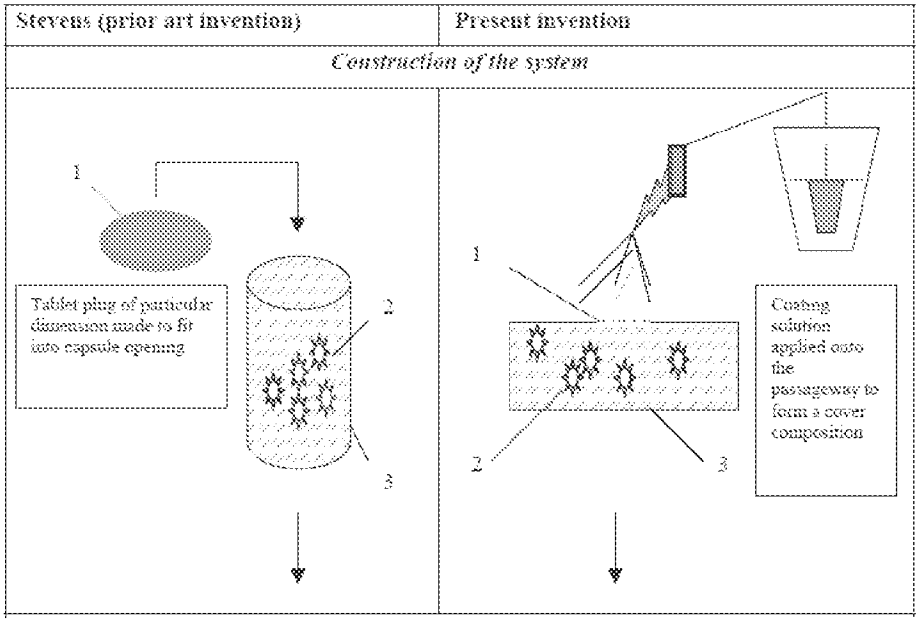
Stevens further provides the following construction details with respect to the orifice in the device and the plug (Stevens at col 3, lines19-31):

> The orifice in the wall of the capsule may adopt any convenient configuration but in the preferred case will be a circular in cross-section and uniform throughout its depth. Such orifices may readily be closed by the insertion of a right cylindrical plug. The delay in the release of the contents of the capsule is dependant to the depth of any particular plug. The device is constructed so as to ensure that the depth of the walls of the orifice is at least equal to the depth of the plug which is required to be accommodated. In the preferred embodiment the plugs may have a depth of from 0.5 to 10.0 mm more preferably 1.0 to 5.0 mm. The plug will preferably be positioned so that its exposed surface is flush with the exterior wall of the capsule.

In a preferred embodiment (See Example 1, lines 50-58), the open ends of the capsule were closed with a tablet formed by compression of Eudragit L100-55 in a die of diameter 7.18 mm to form a tablet having a thickness of 1.27 mm.

Thus, the plug of Stevens is a tablet, not **a cover composition applied in the form of a film so as to substantially cover only the orifice**, as recited in present claim 1.

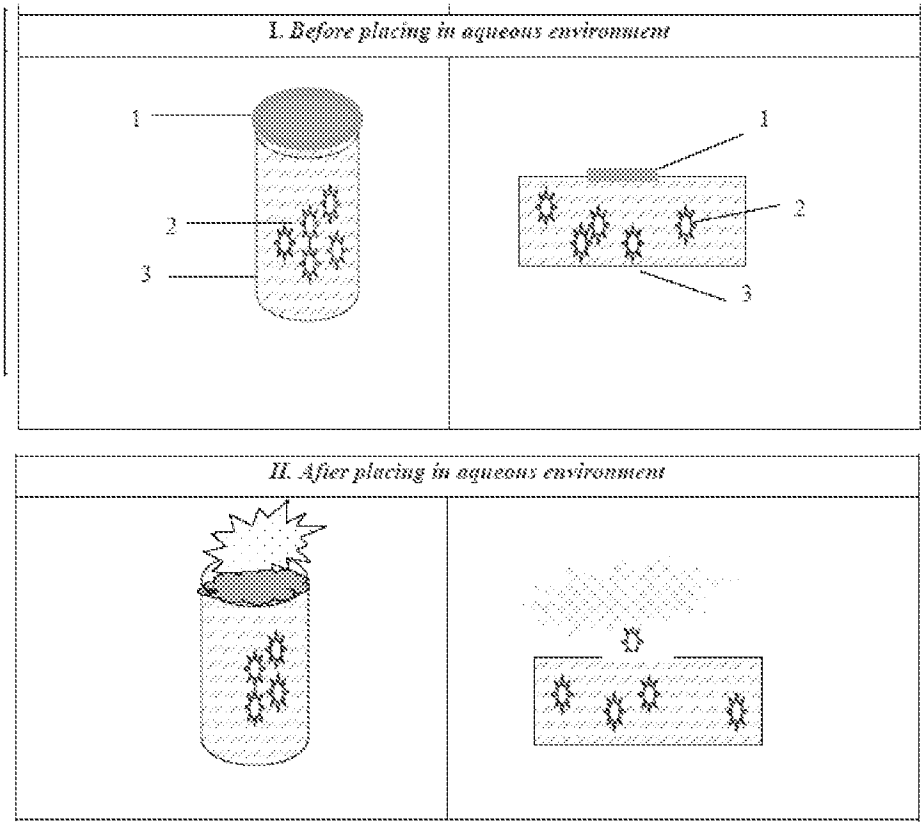
The importance of the differences between the construction of Stevens and the construction of the present invention can be illustrated with the help of the non-limiting schematic drawing below.

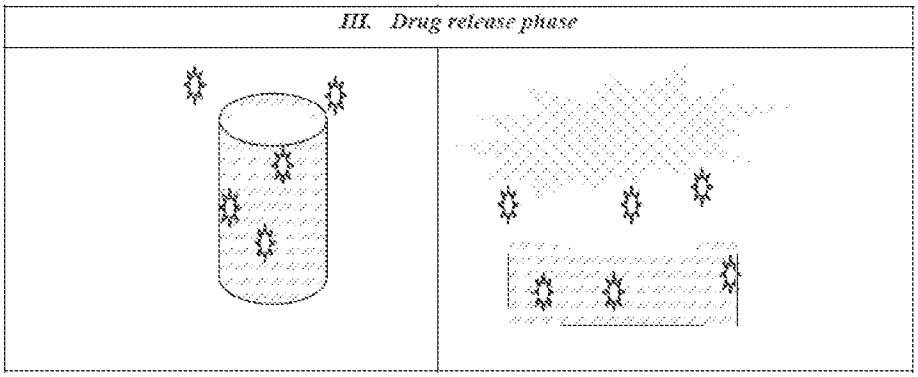


1: Plug (compacted tablet in Stevens / film cover in present invention)
2: Active ingredient core (capsule content in Stevens / compressed core in present invention)
3: Impermeable coat (capsule material in Stevens / coat composition in present invention)

As can be seen from the illustrative drawing, the plug of Stevens is a compacted tablet, with a minimum dimension of a few millimetres. In contrast, the plug of the present invention is in the form of a film (often with a thickness in the order of microns only).

Further, the distinction between how the system of Stevens operates and how the system of the present invention operates is illustrated in the schematic drawing below:





As shown above, the water-soluble plug of Stevens starts to erode after placing in aqueous environment, thereby effecting release of the inner capsule contents after complete erosion of the plug.

In contrast, in the presently claimed invention, the cover composition applied as a film on the passageway starts to dissolve after coming in contact with the gastrointestinal environment, exposing the compressed core to the surrounding aqueous environment, which allows ingress of fluid into the core, thus causing the swelling agent in the core to swell and rupture the coat completely, thereby triggering release of the contents to the external environment. This is not possible with the features of the capsule of Stevens, which relies only on dissolution of its tablet plug and does not cause a core to swell or a coat to rupture.

In summary, in the presently claimed invention, the core composition containing the selected swelling agent, the coat composition, and the plug applied as a film are designed such that, upon contact with the aqueous environment, the swelling agent present in the core composition swells and exerts a pressure on the coat, thereby rupturing the coat to release contents of the core composition, as recited in present claim 1. An advantage of the presently

claimed invention is that the coat is ruptured because of the pressure generated within the core due to the presence of swelling agents.

This is very different from Stevens, where a tablet of compressed material is used to plug a hollow cylinder, and the core does not contain any swelling agent of the type used in the present invention. Namely, Stevens only provides a system where a pulse release of its contents is obtained at a rupture of the plug tablet, not the coat. Therefore, the present claims are not anticipated by Stevens, and not obvious over Stevens.

In addition, with respect to the dependent claims, it is submitted that the combined features of each of these respective claims are not taught or suggested by the cited references. Therefore, each of the dependent claims is not anticipated by Stevens, and not obvious over Stevens.

In view of the above, it is submitted that the rejections should be withdrawn.

Conclusion

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

If there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

If this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to Deposit Account No. 50-2866.

Respectfully submitted,

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